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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,425	03/31/2004	Bruce D. Hammock	02307O-142500US	8475

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EXAMINER	
GRAFFEO, MICHEL	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,425	HAMMOCK ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 9-40 is/are pending in the application.

4a) Of the above claim(s) 11-13,19-24,27-29 and 35-40 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 9,10,14-18,25,26 and 30-34 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, a method of inhibiting progression of obstructive pulmonary disease comprising a urea compound, in the reply filed on 37 March 2006 is acknowledged. No grounds for traversal were presented. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 11-13, 19-24, 27-29 and 35-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

Status of Action

Claims 1-8 have been cancelled pursuant to Applicant's remarks filed 37 March 2006. Claims 9-10, 14-18, 25-26 and 30-34 are examined.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10, 14-18, 25-26 and 30-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing the amount of bronchial lavage cells, i.e. macrophages, comprising treating mice with AUDA-nBE to the extent that the treatment ends at the reduction in cells such as macrophages, as well as for a suggestion to treat acute respiratory distress syndrome via a reduction in leukotoxin with the claimed compounds as shown in mice models (see Morisseau et al. Potent urea and carbamate inhibitors of soluble epoxide hydrolases. Proc. Natl. Acad. Sci 96 (1999) 8849-8854), does not reasonably provide enablement for the inhibition of progression of the scope of obstructive pulmonary diseases included in the scope of the claim nor for the treatment without any specified endpoint. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and ,
8) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) the nature of the invention; the invention is directed to a method of inhibiting progression in a patient of a respiratory diseases but has not recited the step(s) that (a) result in inhibiting nor (b) have a specified end result of the treatment.

2) the breadth of the claims; the scope of the method claims includes the inhibition of progression of obstructive pulmonary diseases comprising any inhibitor of sEH.

3) the predictability or unpredictability of the art; the ability of inhibition of progression of obstructive pulmonary diseases comprising any inhibitors of sEH is not yet known in the art. See for example Bedi "Inhaled Corticosteroids in COPD" Indian J Chest Allied Sci 2005; 47:243-244 which teaches that even post filing of the current Application, that there is no silver bullet for COPD and no drug that can prevent same. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of inhibition of progression of obstructive pulmonary diseases comprising any inhibitor of sEH. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for doing same.

No experimental evidence supporting the contention that the claim specified actives would actually treat these diseases by simply administering the

claim specified active agents has not been demonstrated nor practice the invention without an envisaged endpoint or result of the treatment (note the absence of such recitation in the current claim(s)). The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing and for practicing same without a specific endpoint for the treatment of the claimed diseases.

4) the amount of direction or guidance presented; the specification does not provide any guidance in terms of inhibition of progression of obstructive pulmonary diseases comprising any inhibitor of sEH.

5) the presence or absence of working examples; no working examples are provided for inhibition of progression of obstructive pulmonary diseases comprising any inhibitor of sEH for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the inhibitory effects of the instant compositions. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

6) the quantity of experimentation necessary; the quantity of experimentation would be undue to one of skill in the art and amount to the trial and error type of experimentation without a priori expectation of success. Thus, factors such as "sufficient working examples", "the level of skill in the art" and

"predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. To support a claim to inhibition or the like, Applicant would need to provide confirmative in vivo data supporting the inhibition of progression of the diseases as well as a method and dosage regime resulting in the prevention of same.

In view of the breadth of the claims, the chemical nature of the invention and unpredictability of inhibiting the progression obstructive diseases for example, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 102

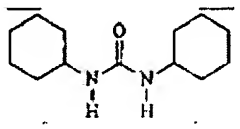
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-10 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Morisseau et al. Potent urea and carbamate inhibitors of soluble epoxide hydrolases. Proc. Natl. Acad. Sci 96 (1999) 8849-8854.

Morisseau et al. teach that treatment with compounds such as DCU having the structural formula below reduce the toxicity of leukotoxin in vivo in mice and prevent symptoms suggestive of acute respiratory distress syndrome (in current claims 9-10 and 14; see Abstract, Discussion page 8852 and 8853):



Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

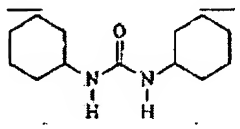
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-10, 14-18, 25-26 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morisseau et al. Potent urea and carbamate inhibitors of soluble epoxide hydrolases. Proc. Natl. Acad. Sci 96 (1999) 8849-8854 in view of Fang et al. Pathways of Epoxyeicosatrienoic Acid Metabolism in Endothelial Cells. The Journal of Biological Chemistry 276(18) 14867-14874 (2001).

Morisseau et al. teach that treatment with compounds such as DCU having the structural formula below reduce the toxicity of leukotoxin in vivo in mice and prevent symptoms suggestive of acute respiratory distress syndrome (in current claims 9-10, and 14-15 and 33-34; see Abstract, Discussion page 8852 and 8853):



Morisseau et al. further reports that the more powerful inhibitors described herein were able to block sEH in vivo in mice (in current claims 15 and 33-34; see on page 8853 in the discussion section) which although does not recite the specifics of the instant claims 15, 33 and 34, does make obvious the instant claims since one of ordinary skill in the art appreciates that to treat a patient, the patient must be administered a safe and effective amount of the active compound.

Morisseau et al. do not teach the treatment of respiratory diseases with both DCU, for example, and an EET.

Fang et al. teach that EETs have anti-inflammatory properties (in current claims 25-26 and 30-34: see Abstract). Specifically, Fang et al. teach 14,15-EET, which is recited in claims 16-18 and 31-32, has anti-inflammatory properties (in current claims 16-18, 25-26 and 31-32; see Abstract and Discussion on page 14873).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach the claimed invention as claimed. One of ordinary skill in the art would have been motivated to combine Morisseau et al. with Fang et al. because combining agents which are known to be useful as anti-inflammatory agents individually into a singe composition useful for the very same purpose is prima facie obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining DCU and an EET flows logically from their having been individually taught in the prior art. Moreover, Fang et al. teach that conversion of 14,15-EET to 14,15-DHET is done by sEH, which in turn means that a reduction in sHE will consequently produce a reduction in 14,15-EET (see Discussion on page 14873). In light of the teaching that EET has beneficial anti-inflammatory properties, one of ordinary skill in the art would find it obvious to maintain the levels of same while inhibiting sHE. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15 May 2006
MG

Ardin H. Marschel 5/15/06
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SUPERVISORY PATENT EXAMINER